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EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 10/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/631,116	DEHNAD, HOUDIN	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *1-26 and 43-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *13 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election **without** traverse of Group II, claims 27-42, and the species 40-O-(2-hydroxy)ethyl-rapamycin in the reply filed on 9/15/2006 is acknowledged.

Claims 1-26 and 43-48 are withdrawn from further consideration pursuant to 37 CFR § 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/15/2006.

Status of the Claims

Claims 1-48 are currently pending. Claims 1-26 and 43-48 are withdrawn from consideration. Claims 27-42 are under examination and are the subject of this Office Action. This is the first Office Action on the merits of the application.

Priority

This application does not claim the benefit or priority to any prior filed U.S. or foreign applications. As such, the earliest effective U.S. filing date for prior art purposes is 7/31/2003.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 11/14/2003 has been considered to the extent that each reference cited therein is a proper citation. The lined-through references were not considered because they are not proper citations. Many of these references only cite the date they were printed from the Internet, not the date they were first published (*e.g.* Reference C1).

This is insufficient for examination purposes because the publication date is necessary for determination of applicable prior art. Further, other lined-through references do not have a date at all (*e.g.* Reference C15) while others are missing the source of the publication (*e.g.* Reference C32). Please see attached Form 1449. Also see 37 C.F.R. § 1.98(b)(5).

Claim Rejections - 35 USC § 112 – First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34 and 39 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant case, claim 34 recites a barrier layer that "is of the type that substantially prevents diffusion of the active agent from the coating". Claim 34 is dependent from claim 33, wherein the barrier is said to comprise "a polymer." There is insufficient written description for polymers of the "type" that substantially prevents diffusion of an active agent from the coating. Although the specification describes numerous polymers (page 32), there is no specific description of the structural features required to prevent diffusion of active agents.

Claim 39 recites a fluid "capable of removing polymer fragments from the coating." As discussed *supra,* there is insufficient written description for this functional limitation whereby a

fluid is defined by its capability. As with the polymers discussed previously, although the specification describes several fluids, including etchants and organic solvents, there is no description of specific fluids or fluid characteristics that are capable of removing polymer fragments from a coating. As such, it is not clear that applicant had possession of all fluids capable of performing this function and the specification fails to describe a sufficient number of species from this genus to demonstrate possession of the claimed invention.

M.P.E.P. § 2163 states, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention...one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process." While the specification describes several polymers and "fluids", it does not describe a sufficient number of species as to convey possession of the entire genus encompassed by the functional limitations recited in claims 34 and 39.

Claim Rejections - 35 USC § 112 – Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-42 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 27, 28 and 29 recite the limitation "less than about" with respect to residual fluid content. This limitation renders the claim indefinite because the phrases "less than" and "about", when used together, simultaneously limit and broaden the intended range, thus rendering the metes and bounds of the limitation unclear. For example, "less than 10%" is clear and indicates a finite range. However, "less than about 10%" expands the range, but to what extent is unclear. Applicant has not defined what is meant by the term "about" in the specification. Thus, the skilled artisan is not apprised of the metes and bounds of the claim limitation. Claims dependent from claims 27, 28 and 29 are included in this rejection.

Claim 27 recites a composition, the composition "including a polymer, an active agent and a solvent." The word "including" renders the claim indefinite because it is not clear what else is included in the composition. Amending the claim to recite "the composition *comprising*..." would overcome this rejection.

Claims 32 and 38 recite the limitation "the stent" in line 2 of each respective claim. There is insufficient antecedent basis for this limitation in the claims.

Claims 33-35 recite the limitation "substantially" at various lines in the claims. This limitation is indefinite because it is not clear to what extent the polymer is free of active agent (claims 33 and 35) or to what extent a barrier prevents diffusion of active agent (claim 34). Does "substantially" mean less than 1%? 10%? 20%?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 27-30 and 33-36 are rejected under 35 U.S.C. § 102(b) as being anticipated by Ding *et al.* (U.S. Patent No. 5,837,313; prior art of record).

The instant claims are drawn to a method of manufacturing a drug eluting implantable medical device, comprising applying a composition comprising a polymer, an active agent and a solvent, allowing the solvent to evaporate and subsequently directing a beam of charged particles to the dry polymeric coating.

Ding *et al.* teach a method of coating an implantable open lattice metallic stent comprising sequentially applying a plurality of relatively thin outer layers of a coating composition comprising a solvent mixture of uncured polymeric silicone material and crosslinker and finely divided biologically active species. The coatings are cured and subjected to argon gas plasma and exposure to gamma radiation electron beam, ethylene oxide, and steam (Abstract). Polymers suitable for the coatings taught in the reference include polyurethanes as instantly claimed (col. 4, lines 48-62). The solvent is evaporated in the curing process, often at elevated temperatures (col. 8, lines 21-37). Such evaporation will inherently result in the residual solvent percentages instantly claimed. Argon plasma treatment and subsequent exposure to gamma radiation (col. 8, line 48 to col. 9, line 8) meet the instant limitation of "directing a beam of charged particles" to the dry polymeric coating. With respect to instant claims 33-35, which

recite forming a barrier layer of polymer comprising no active agent, the reference teaches that multiple layers may be employed wherein one or may layers do not contain active agent (col. 10, lines 50-59).

The reference thus teaches all of the limitation of the instant claims.

Claims 27-29 and 33-36 rejected under 35 U.S.C. § 102(e) as being anticipated by anticipated by Hossainy *et al.* (U.S. Patent No. 6,713,119; Issued Mar. 30, 2004; Filed Dec. 23, 1999).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. § 102(e). This rejection under 35 U.S.C. § 102(e) might be overcome either by a showing under 37 CFR § 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR § 1.131.

Hossainy *et al.* teach coatings for a prosthesis (*e.g.* stent) comprising a polymer, solvent and therapeutic substance (Abstract; Examples). Ethylene vinyl alcohol copolymer may be used as a polymer (col. 2, lines 62-67). The solvent(s) are removed by heating thereby allowing the components to "evaporate to substantial elimination" (col. 4, lines 1-7). The reference also teaches application of a second layer comprising a polymeric material without a therapeutic substance (col. 4, lines 8-15). With regard to the method step of "directing a beam of charged particles to the dry polymeric coating" the reference teaches that the coated stents may be sterilized by "electron beam radiation" (col. 12, lines 23-25).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 27-30, 33-36, 39 and 41 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ding *et al.* (U.S. Patent No. 5,464,650; prior art of record) in view of Yang *et al.* (U.S. Patent No. 6,120,847; Issued Sept. 19, 2000).

Ding *et al.* teach as discussed *supra*. The reference does not disclose exposing the dry coating to a fluid to remove polymer fragments from the coating as required by the limitations of claims 39 and 41.

However, Yang *et al.* disclose a surface treating method for stent coating that eliminates surface imperfections on a medical device having a drug release coating including a therapeutic substance in a polymeric carrier disposed on at least a portion of the medical device (Abstract). The polymers used in the coatings include the instantly claimed poly(L-lactide) (col. 3, lines 31-44). The applied coating comprises a solvent, a polymer, and a therapeutic agent and the solvent is evaporated to leave on the stent surface a coating of the polymer and the therapeutic agent (col. 4, lines 1-2 and 24-27). Because the procedures for applying the polymeric surface treatments leave polymeric fibers, polymeric particles or other polymeric surface aberrations, there is a need to eliminate or reduce the unwanted imperfections. As such, Yang *et al.* disclose a method of contacting a coated stent having polymeric imperfections with a vaporized solvent (col. 5, lines 18-35). Organic solvents can be used and it is anticipated by the reference that not

only the vapor, but also the fluid itself can be used to remove polymer imperfections (col. 5, lines 36-44 and 57-60).

In the absence of a showing of unexpected results commensurate in scope with the claims, the instantly claimed methods would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Yang *et al.* provide the motivation to contact a coated stent with an organic solvent wherein it is disclosed that such contact can remove polymeric imperfections from the coated stent.

Claims 27-30 and 32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Berg *et al.* (U.S. Patent No. 5,464,650; prior art of record) in view of Han *et al.* (prior art of record).

The instant claims are drawn to a method of manufacturing a drug eluting implantable medical device, comprising applying a composition comprising a polymer, an active agent and a solvent, allowing the solvent to evaporate and subsequently directing a beam of charged particles to the dry polymeric coating.

Berg *et al.* disclose a method of making an intravascular stent (*i.e.* an implantable medical device) comprising applying to the body of the stent a solution comprising a solvent, a polymer, and a therapeutic substance and then evaporating the solvent (Abstract; col. 3, lines 52-66). The inclusion of a polymer allows the drug to be retained on the surface of the stent and further allows for the slow administration of drug (col. 2, lines 36-40). The solution of polymer, drug, and solvent is applied to the stent and the solvent is evaporated, thereby leaving on the stent surface a coating of the polymer and the therapeutic substance (col. 4, lines 19-22).

With regard to instant claims 27-29, which recite specific percentages of residual solvent, although the reference dose not explicitly state such percentages, it is very clear that the inventors mean complete evaporation of solvent. The fact that the solvent is evaporated "thereby leaving on the stent surface a coating of the polymer and the therapeutic substance" supports this interpretation.

With regard to instant claim 30, which recites specific polymers, Berg *et al.* disclose identical polymers that may be used in the described invention, including poly(L-lactic acid), poly(glycolic acid) and poly(vinylidene fluoride) (col. 4, line 35 to col. 5, line 7). It is noted that the instantly claimed polymers are well known in the art as coatings for implantable medical devices.

Berg *et al.* do not disclose directing a beam of charged particles to the dry polymeric coating.

However, Han *et al.* discuss the use of synthetic polymers, including the instantly claimed poly(vinylidene fluoride) and poly(tetrafluoroethylene) and their use in chemically resistive tubes, vessels and container walls due to their chemical inertness (page 4327, left column). There have been many attempts to modify the surface of these polymers to improve wetting, dye printing and adhesion to another phase (*id.*). Techniques to modify the surface of said polymers have included plasma technology, high-energy ion beam irradiation and other techniques. Han *et al.* disclose the irradiation of poly(vinylidene fluoride) and poly(tetrafluoroethylene) with argon ions in an oxygen environment. Said Ar^+ ions were at a fixed ion beam current of 5×10^{14} to 1×10^{17} Ar^+/cm^2 (page 4327, right column). These irradiating ions induced chemical changes in the polymeric chains. For example, the surface of

poly(vinylidene fluoride) became "rougher" and resulted in changed wetting properties (page 4331).

In the absence of a showing of unexpected results commensurate in scope with the claims, the instantly claimed method would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Polymeric coatings containing therapeutic agents for implantable medical devices were well known in the art as evidenced by Berg *et al.* It was also known that irradiating with charged ions as described in Han *et al.* could modify the chemical and structural properties of the polymers used in said polymeric coatings. The skilled artist would have been motivated to irradiate the polymers disclosed in Berg *et al.* using the techniques described in Han *et al.* because such irradiation would be expected to lead to improved wetability and structural changes resulting in altered release of therapeutic agents.

Claims 33-35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Berg *et al.* and Han *et al.* as applied to claims 27-30 and 32 above, and further in view of Tuch (U.S. Patent No. 5,624,411; prior art of record).

Berg *et al.* and Han *et al.* disclose as discussed *supra*. Neither reference discloses forming a "barrier layer" over the dry coating wherein the barrier layer comprises a polymer free of active agent.

However, Tuch discloses a method of making an intravascular stent by applying to the body of the stent a therapeutic substance and then overcoating the therapeutic substance with a porous polymer (Abstract). The methods described in Tuch are similar to those described in Berg *et al.*, however an additional step of applying an "overlayer" is disclosed. This overlayer

provides additional control over the elution of the drug (col. 6, lines 32-33). Further, it is disclosed that the overlayer(s) use the same polymer used in the application of polymer and drug (col. 6, lines 42-44).

Thus, the application of additional polymer without drug to form a "barrier" would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Such a barrier would be expected to prevent diffusion of active agent as demonstrated in Tuch (see especially Figure 3).

Claims 37-38 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Berg *et al.* and Han *et al.* as applied to claims 27-30 and 32 above, and further in view of EP 0970711 (prior art of record).

Berg *et al.* and Han *et al.* disclose as discussed *supra*. Neither reference discloses masking a portion of the coating prior to directing the beam of charged particles to eliminate or reduce the exposure of charged particles to the portion of the coating covered by the mask.

However, EP '711 discloses a method of controlling the thickness of a polymer coating applied to the inner surface of a stent by fitting a mandrel within its interior (¶ [0006]). This mandrel is disclosed to minimize or eliminate polymer coating on the inner surface of the stent. EP '711 also discloses the same polymeric coating instantly claimed (¶ [0023] to [0025]) as well as a polymeric coating comprising the therapeutic agent rapamycin (¶ [0030] and Example 7).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the mandrels disclosed in EP '711 to protect the inner surface of an implantable medical device (*e.g.* a stent) from the irradiation disclosed in Han *et al.* One skilled

in the art would be motivated to do so because EP '711 discloses that it is often desirable for the inner and outer surfaces of implantable stents to have different properties, including drug elution profiles. Further, it would have been prima facie obvious to substitute an analog of rapamycin as disclosed in EP '711 as the therapeutic agent present in the disclosures of the prior art. One skilled in the art would have a reasonable expectation that a structural analog of rapamycin, such as the instantly claimed 40-O-(2-hydroxy)ethyl-rapamycin, would have the same or better immunosuppressive effects as the parent compound rapamycin. Further, the skilled artisan would have been imbued with at least a reasonable expectation that exposure of the outer polymer to argon irradiation while protecting the inner polymer from said irradiation, would result in different chemical and structural properties of the respective polymers.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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October 4, 2006

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